REMARKS

Interview Summary And Election

On July 15, 2005, Examiner Goddard called the undersigned attorney requesting a telephone restriction in the above case. According to Examiner's Goddard's request, the undersigned attorney affirms the election of Group I, claims 1-9 and SEQ ID NO: 9. This election is made without traverse.

In view of the restriction requirement, Applicants have amended claims 1, 3, and 6 to recite SEQ ID NO: 9 and complements thereof. Applicants reserve the right to file one or more divisional applications to the remaining inventions.

Claim Amendments

Claims 1, 2, and 6 have been amended to recite that the method is for detecting the presence of a target prostate cancer associated (PS112) polynucleotide in a test sample. Support for the phrase "prostate cancer associated" can be found, for example, on page 9, line 36 through page 10, line 8 of the specification. Also, in claim 1, in step b), the phrase "wherein said target-specific polynucleotide specifically hybridizes to said test sample" has been added. Support for this phrase can be found, for example, on page 24, line 19 through page 25, line 12; page 26, lines 8-36, of the specification. Also, in claim 1, in step b), the phrase "said complements having a length and a sequence of at least 15 nucleotides" has been added. Support for this phrase can be found on page 11, lines 17-24 of the specification. Also, the required percent identity in all claims was amended from 50% to 80%. Support for this change can be found on page 22, lines 26-28 of the specification.

Claim 3 has been amended to recite that the method is for detecting target prostate cancer associated (PS112) mRNA in a test sample. Support for the phrase "prostate

cancer associated" can be found on page 9, line 36 through page 10, line 8 of the specification.

Rejection of Claims 1-9 Under 35 U.S.C. §112, First Paragraph

The Examiner rejects claims 1-9 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. According to the Examiner, "the claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." (See Office Action mailed 07/21/2005, p. 5.) The Examiner further states that the written description is satisfied only for the PS112-specific polynucleotide or oligonucleotide wherein said polynucleotide or oligonucleotide comprises SEQ ID NO: 9. *Id.* Applicants respectfully disagree and traverse this rejection as follows.

Applicants would like to point out that claim 1 is currently drawn to a method of detecting the presence of a target prostate cancer associated (PS112) polynucleotide in a test sample comprising contacting the sample with a PS112-specific polynucleotide or complement thereof, and detecting the presence of said target PS112 polynucleotide, wherein said PS112-specific polynucleotide has at least 80% identity to a polynucleotide selected from the group consisting of SEQ ID NO: 9 and complements thereof, said complements have a length and a sequence of at least fifteen nucleotides.

The term "complements" is well known in the art to be those sequences that are complementary to a polynucleotide sequence. "Complementarity" is defined by Lodish et al., *Molecular Cell Biology, Fourth Edition* (W.H. Freeman and Company, 2000) as "referring to two nucleic acid sequences or strands that form a perfect base-paired double helix with each other."

There is a strong presumption that when an application is filed, an adequate written description is present. *Manuel of Patent Examining Procedure* ("MPEP") §2163 (8th Edition, October 2005 Revision). When a question regarding the adequacy of the written description arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art, as of the filing date sought, that applicant was in possession of the invention as now claimed. MPEP §2163.02. Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. *Id.*

The Examiner states that to provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. (See Office Action, p. 5.) With respect to this point, Applicants wholeheartedly agree. However, the Examiner then takes the position that "the specification does not directly describe PS112-specific polynucleotides, polynucleotide complements, or oligonucleotides with 50% identity to SEQ ID NO: 9 or fragments or complements thereof as useful in the claimed invention in a manner that satisfies either the *Lilly* or *Enzo* standards." *Id.* Applicants respectfully disagree.

First, Applicants note that the amended claims recite polynucleotides, polynucleotide complements or oligonucleotides having at least 80% identity to SEQ ID NO: 9. Support for this language is found in the specification on page 22, lines 26-28 ("preferably at least 70% and more preferably at least 90% identity"). Applicants continue to believe that hybridization of the polynucleotides to target sequences will occur even if there is 50% identity between the polynucleotide and the sequence; however, in an effort to expedite prosecution, Applicants have increased the percent identity language to at least 80%.

Second, Applicants are a little puzzled by the Examiner's choice of the word "useful" in connection with the written description rejection. *Id.* Applicants respectfully submit that usefulness is not a factor for the written description requirement, as there is a separate statutory requirement for usefulness. Neither the case law nor the USPTO Written Description Guidelines provide that the written description requirement encompasses a showing of usefulness. If the Examiner really believes that the usefulness requirement is not met, she should have issued a §101 rejection. Since the Examiner has not issued a §101 rejection, Applicants assume that the invention is deemed useful, as it should be and is.

Third, Applicants submit that the specification adequately describes the methods encompassed within the scope of the invention being claimed. Applicants respectfully disagree with the Examiner's apparent belief that there are two separate standards to meet the written description requirement: the *Lilly* standard and the *Enzo* standard. Applicants believe that the proper standard for the written description requirement was explained by the Federal Circuit in *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 296 F.3d 1316, 63 USPQ2d 1602 (Fed. Cir. 2002) where the Court adopted a portion of the Written Description Guidelines:

> The written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics...i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of characteristics. *Id.*, at 1324 (citations omitted).

In this regard, Applicants draw the Examiner's attention to a recent decision by the Board of Patent Appeals and Interferences, *Ex parte Bandman et al.*, Appeal No. 2003-1805, Application No. 09/079,892 (May 25, 2004).[1]

[1] Applicants are aware that this decision and other BPAI decisions cited in this Amendment were not written for publication and are not binding precedent of the Board. Nevertheless, Applicants believe that the decisions are highly relevant as they illustrate the position of the BPAI on the written description in very similar cases. Copies of all cited BPAI cases are enclosed with this Amendment.

In *Bandman*, representative claims 3 and 12 were as follows:

> 3. An isolated polynucleotide encoding a polypeptide selected from the group consisting of:
>
> a) a polypeptide comprising the amino acid sequence of SEQ ID NO: 1; and
>
> b) a polypeptide comprising a naturally occurring amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 1.
>
> 12. An isolated polynucleotide encoding a polypeptide selected from the group consisting of:
>
> a) a polynucleotide comprising the polynucleotide sequence of SEQ ID NO: 2,
>
> b) a polynucleotide comprising a naturally occurring polynucleotide sequence at least 95% identical to the polynucleotide sequence of SEQ ID NO: 2,
>
> c) a polynucleotide having a sequence complementary to a polynucleotide of a),
>
> d) a polynucleotide having a sequence complementary to a polynucleotide of b) and
>
> e) an RNA equivalent of a)-d).

According to the BPAI, the Examiner in *Bandman* issued a written description rejection contending that the specification provided only a single representative species—an isolated polynucleotide consisting of SEQ ID NO: 2. The rejection asserted that "[t]here is no disclosure of any particular structure to function/activity relationship in the single disclosed species." The rejection concluded that "[g]iven this lack of additional representative species as encompassed by the claims, [appellants] have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize [appellants] were in possession of the claimed invention." *Bandman*, p. 3.

The BPAI explained that in *Enzo Biochem*, the Federal Circuit refined the *Lilly* approach, holding that adequate written description may be present for a genus of nucleic

acids based on their hybridization properties, if "they hybridize under highly stringent conditions to known sequences because such conditions dictate that all species within the genus will be structurally similar." *Id.*, p. 4, citing *Enzo Biochem*, 296 F.3d at 1327, 63 USPQ2d at 1615. The BPAI noted that the specification fully described the complete structure of the polynucleotide of SEQ ID NO: 2 and that the genus was limited to a polynucleotide comprising a naturally occurring polynucleotide sequence at least 95% identical to the polynucleotide sequence of SEQ ID NO: 2. The Board further noted that the complete structure of the polypeptide of SEQ ID NO: 1 has been described and that the genus was limited to polypeptides comprising a naturally occurring amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 1. Therefore, the BPAI reversed the written description rejection of all claims.

The claims rejected in the instant application are highly similar to the claims in *Bandman*. If anything, there is more written description of the pending method claims. Claim 1 of the instant application recites a method of detecting the presence of a target prostate cancer associated (PS112) polynucleotide in a test sample comprising contacting the sample with a PS112-specific polynucleotide or complement thereof, and detecting the presence of said target PS112 polynucleotide, wherein said PS112-specific polynucleotide has at least 80% identity to a polynucleotide selected from the group consisting of SEQ ID NO: 9 and complements thereof wherein said complements have a length and sequence of at least fifteen nucleotides. The specification discloses the complete structure of SEQ ID NO: 9, explains how to identify PS112 gene-specific clones (Example 1), how to sequence PS112 EST-specific clones (Example 2), how to prepare PS112 nucleic acid (Example 3), and how to confirm the hybridization of labeled probes to targets (Examples 4-7).

The fact that the specification does not expressly describe various polynucleotides having at least 80% identity to SEQ ID NO: 9 does not mean the written description requirement is not met. As the BPAI in *Bandman* recognized, "the written description requirement of 35 U.S.C. §112, first paragraph, does not require a description of the

complete structure of every species within a chemical genus." *Id.*, citing *Utter v. Hiraga*, 845 F.2d 993, 998, 6 USPQ2d 1709, 1714 (Fed. Cir. 1988). Because the level of skill in the area of molecular biology is high, one of ordinary skill in the art would clearly recognize that Applicants have provided an adequate written description of PS112-specific polynucleotides, oligonucleotides and complements that have at least 80% identity to SEQ ID NO: 9. As in *Bandman*, the genus claimed in the instant application is limited; Applicants only claim methods involving the use of polynucleotides with at least 80% identity to SEQ ID NO: 9. As the specification discloses on page 10, lines 14-29, techniques to determine nucleic acid and amino acid sequence identities are well known in the art. There are several programs available, such as the Wisconsin Sequence Analysis Package and the GAP program, that are capable of calculating both the identity between two polynucleotides and the identity and similarity between two polypeptide sequences.

It is irrelevant that, as the Examiner claims, SEQ ID NO: 9 contains 2,393 nucleotides which would comprise thousands of possible fragments or complements. Applicants have amended the claims to delete the reference to fragments and the term "complement" is readily understood by those with an ordinary skill in the art as a complementary sequence to a nucleotide sequence. Moreover, Applicants limited the claims to recite that the complements be of at least fifteen nucleotides, further limiting the claimed genus.

To further illustrate that the claims reciting percent identity and complements satisfy written description requirement, Applicants draw the Examiner's attention to another BPAI case, *Ex Parte Sun*, Appeal No. 2003-1993, Application No. 09/470,526 (January 20, 2004).

Representative claim 31 is as follows:

> 31. An isolated wee1 nucleic acid comprising a member selected from the group consisting of:
>
> a) a polynucleotide that encodes a polypeptide of SEQ ID NO: 2;
> b) a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO: 1;
> c) a polynucleotide comprising the coding sequence set forth in SEQ ID NO: 1; and
> d) a polynucleotide complementary to a polynucleotide of (a) through (c).

Ex Parte Sun, pp.1-2.

The invention at issue was directed to corn plant nucleic acids and their encoded proteins which are involved in cell cycle regulation. The Examiner in this case argued that one skilled in the art

> "could not predict the structure and function of isolated nucleic acids comprising a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO: 1 or a polynucleotide complementary thereto, or cells, plants, and seeds transformed therewith. The physical features of the claimed isolated nucleic acids and transgenic cells, plants, and seeds cannot be ascertained in the absence of information about the functional activities of these nucleic acids. Additionally, the specification does not disclose the effect of incorporating the claimed isolated nucleic acids into the genome of a cell or plant." *Id.*, p. 7.

The Examiner also pointed to the fact that the specification did not teach a single representative species with 80% identity and wee1 function.

The Board found confusing the Examiner's interjecting predictability in the context of a written description rejection, "as predictability is not the legal standard or test for such rejections." *Id.* Citing the standard enunciated in *Enzo Biochem*, the Board rejected the Examiner's contention that the claims did not satisfy the written description requirement:

> ...we do not find the fact that the specification does not specifically teach the structure of a species with 80% identity and WEE1 function to be dispositive of the written description issue here.
>
> The specification specifically describes the chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO: 2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO: 1. The specification also provides an example of how to screen for WEE1 activity, specification, Example 1, pages 33-34 and Example 3. Contrary to the examiner's position, it would reasonably appear that such a description in the specification would constitute sufficiently detailed, relevant identifying characteristics of the claimed subject matter consistent with Enzo (supra)....
>
> We agree with appellants that the examiner has not established with a preponderance of the evidence, that the combination of the disclosure of the specific chemical structures of a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, as well as teachings in the specification on how to test for wee1 activity and teachings of the areas of the wee1 gene that can be altered without disturbing substrate recognition are insufficient to describe a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO: 1. What is evident from the record is those of ordinary skill in the art were aware that most of the variations in amino acid sequences of WEE1 are in the amino terminus, while the carboxy end of the genes are relatively conserved. *Ex Parte Sun*, pp. 9-10.

Applicants submit that the claims pending in the instant application are highly similar to the claims in *Ex Parte Sun*. For example, claim 1 of the instant application recites a method of detecting the presence of a target prostate cancer associated (PS112) polynucleotide in a test sample comprising contacting the sample with a PS112-specific polynucleotide or complement thereof, and detecting the presence of said target PS112 polynucleotide, wherein said PS112-specific polynucleotide has at least 80% identity to a polynucleotide selected from the group consisting of SEQ ID No: 9 andor complements thereof, said complements having a length and sequence of at least fifteen nucleotides. The Examiner's stated reasons for the written description rejection include the recitation in the claims of percent identity and of complements. However, percent identity and complements were recited in claims in *Ex Parte Sun* and the BPAI reversed the written description rejection in that case. In the instant application, Applicants disclose the

complete structure of SEQ ID NO: 9 and explain how to use a polynucleotide having 80% identity to SEQ ID NO: 9 to detect the presence of a target PS112.

Moreover, as opposed to the instant case, in *Ex Parte Sun*, the Examiner at least relied on a reference that suggested that specific amino acids residues of WEE1 were critical to the function of the regulatory domain. The Examiner reasoned that changes in those residues could have had an effect on WEE1 function, and since the claims in dispute allowed for 80% identity throughout the sequence, he rejected the claims on written description grounds. As explained above, the rejection was nevertheless reversed by the BPAI. However, in the instant case, the Examiner cites no evidence that specific parts of PS112 sequence are more critical than the other parts of the same sequence. Therefore, there is no scientific evidence that a sequence having at least 80% identity to SEQ ID NO: 9 would not be able to hybridize to a test sample, as mere speculation that mutations may involve critical regions is insufficient to reject the claims. "A general allegation of unpredictability in the art is not a sufficient reason to support a rejection for lack of adequate written description." MPEP §2163.04.

Applicants draw the Examiner's attention to yet another BPAI case, *Ex Parte Meyers*, Appeal No. 2003-1820, Application No. 09/464,039 (August 31, 2004).

Representative claims 77 and 88 are as follows:

77. A method for detecting the presence of a nucleic acid molecule of claim 87 in a sample, said method comprising the steps of contacting the sample with a nucleic acid probe which selectively hybridizes to the nucleic acid molecule and determining whether the nucleic acid probe binds to the nucleic acid molecule in the sample; wherein said nucleic acid probe is selected from the group consisting of:

a) the nucleotide sequence set forth in SEQ ID NO: 8;
b) the nucleotide sequence of a fragment of the nucleotide sequence set for[th] in SEQ ID NO: 8, wherein said fragment comprises at least 417 contiguous nucleotides of the nucleotide sequence set forth in SEQ ID NO: 8;
c) a nucleotide sequence having at least 70% sequence identity to the nucleotide sequence set forth in SEQ ID NO: 8; and
d) a nucleotide sequence complementary to a nucleotide sequence of a), b), or c).

88. An isolated nucleic acid molecule having a nucleotide selected from the group consisting of:

a) a nucleotide sequence encoding a polypeptide having dehydrogenase activity, wherein said nucleotide sequence has at least 70% sequence identity with the nucleotide sequence set forth in SEQ ID NO:8; and
b) a nucleotide sequence complementary to the nucleotide sequence of a).

Claim 87 recited an isolated nucleic acid molecule comprising, *inter alia*, the nucleotide sequence set forth in SEQ ID NO: 8. *Ex Parte Meyers*, pp. 1-2.

SEQ ID NO:8 encoded the novel 21612 polypeptide which was determined to belong to the short chain alcohol dehydrogenase family. *Id.*, pp. 5-6.

The Examiner rejected claim 88 on written description grounds.

According to the examiner (Answer, page 6) claims 88-92 "are drawn to a nucleotide sequence encoding a polypeptide having dehydrogenase activity,

> wherein the nucleotide has at least 70-90% sequence identity with [the] nucleotide sequence of SEQ ID NO: 8." In this regard, the examiner finds (id.), "[t]he specification as [filed] fails to disclose any and all variant [sic] of human alcohol dehydrogenase comprising the nucleic acid sequence of SEQ [ID NO:] 8, which encodes the amino acid sequences [sic] of SEQ ID NO: 7." *Ex Parte Meyers*, pp. 14-15.

The Examiner asserted that "the 21612-polynucleotides has [sic] been defined only by a statement of function of short chain alcohol dehydrogenase activity, which conveyed no distinguishing information about the identity of the claimed DNA sequence, such as its relevant structural or physical characteristics." According to the Examiner (Answer, page 7), appellant discloses SEQ ID NO: 8, and "proposes to discover other members of the genus using hybridization procedure [sic]. *Id.*, p. 15

The Board reversed, agreeing with the appellant that a) the Examiner presented no evidence that a person skilled in the art would doubt the credibility of applicant's assertion that the 21612 polypeptide functions as a dehydrogenase, and b) claims 88-92 recite the identifying structural characteristics that identify each genus of nucleotide sequences. *Id.*, pp. 15-16.

> Further, as appellant points out (Brief, page 15), the claims are limited to nucleotide sequences meeting both the structural requirements of these claims and the claimed functional requirement—having dehydrogenase activity. Both appellant's and the examiner's Pfam analysis (see Answer, page 9) demonstrate that a person of ordinary skill in the art at the time the invention was made would recognize the relevant structural characteristics of appellants' claimed invention that are necessary to place a polypeptide encoded by a nucleic acid variant of SEQ ID NO: 8 in the dehydrogenase family of proteins. *Id.*, p. 17.

The Board also noted that the Examiner did not issue a written description rejection for claim 77 despite that it also contains similar % identity language. *Id.*

The structure and the nature of the claims in the instant invention are highly similar to those of the claims in *Ex Parte Meyers*. Similar to claim 77 in that case, Applicants' claim 1 recites a method for detecting the presence of a polynucleotide

(claim 77 recites detecting the presence of a nucleic acid molecule). As in claim 77, Applicants recite contacting a test sample with a probe which selectively hybridizes to a target. While claim 77 of *Ex Parte Meyers* recited that the probe may have a nucleotide sequence of at least 70% identity, claim 1 requires 80% identity. While in *Ex Parte Meyers*, the inventors determined by a computer analysis that SEQ ID NO: 8 most likely encodes alcohol dehydrogenase, Applicants in the instant case determined that SEQ ID NO: 9 is predominantly expressed in prostate tumor tissues, thus serving as useful marker for prostate cancer. Therefore, as in *Ex Parte Meyers*, Applicants determined a useful function of a protein encoded by SEQ ID NO: 9: to serve as a marker for prostate cancer.

Therefore, it is instructive that the Board in *Ex Parte Meyers* found that the claims reciting polynucleotides having 70% identity to the disclosed sequence satisfied the written description requirement despite the fact that no other variants were disclosed.

Thus, in all three BPAI cases: *Ex Parte Bandman*, *Ex Parte Sun*, and *Ex Parte Meyers*, the Board reversed written description rejections entered under similar justifications as in the present case. Notably, the Board stressed that in cases of percent identity, under the *Enzo Biochem* standard, it is not necessary to disclose every species of a claimed genus; in neither of these cases, did applicants disclose any variants of the disclosed sequences. Nevertheless, claims reciting percent identity were found to satisfy the written description requirement.

Applicants maintain that by disclosing the full structure of SEQ ID NO: 9, its useful function as a marker for prostate cancer, the methods of making and using the sequence and the nucleic acids that it encodes; the computer programs that make it routine to determine percent identity, and given the high skill in the art, Applicants disclosed a representative number of species so that a person skilled in the art would determine that Applicants were in possession of the claimed invention.

Therefore, Applicants respectfully request that the written description rejection of claims 1-9 be reconsidered and withdrawn.

Double Patenting Rejection

The Examiner rejected claims 1-9 under the doctrine of obviousness-type double patenting over claims 1-9 of U.S. Patent No. 6,110,675. Applicants will submit a Terminal Disclaimer upon notice by the Patent Office of allowable subject matter.

CONCLUSION

Applicants respectfully submit that the claims comply with the requirements of 35 U.S.C. Section 112. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

Should the Examiner have any questions concerning the above, she is respectfully requested to contact the undersigned at the telephone number listed below. If the Examiner notes any matters which the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned.

If any additional fees are incurred as a result of the filing of this paper, authorization is given to charge Deposit Account No. 23-0785.

Respectfully submitted,
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